

WE CLAIM:

1. A method of measuring analyte concentrations in bodily fluids, comprising the steps of:

- a) focusing a laser beam with sufficient energy fluence to ablate the skin at least as deep as the stratum corneum, but not as deep as the capillary layer;
 - b) firing the laser to create a site of ablation, the site having a diameter of between 0.5 microns and 5.0 cm;
 - c) collecting a sample of interstitial fluid released by steps (a) and (b);
- and
- d) testing the interstitial fluid for analyte concentration.

2. The method of claim 1 wherein the laser beam has a wavelength of 0.2 - 10 microns.

3. The method of claim 1 wherein the laser beam has a wavelength of between 1.5-3.0 microns.

4. The method of claim 1 wherein the laser beam has a wavelength of about 2.94 microns.

5. The method of claim 1 wherein the laser beam is emitted by a laser selected from the group consisting of Er:YAG, pulsed CO₂, Ho:YAG, Er:YAP, Er/Cr:YSGG, Ho:YSGG, Er:GGSG, Er:YLF, Tm:YAG, Ho:YAG, Ho/Nd:Yal₀3, cobalt:MgF₂, HF chemical, DF chemical, carbon monoxide, deep UV lasers, and frequency tripled Nd:YAG lasers.

6. The method of claim 1 wherein the laser beam is emitted by an Er:YAG laser.

7. The method of claim 1 wherein the laser beam is emitted by a modulated laser selected from the group consisting of continuous-wave CO₂, Nd:YAG, Thallium:YAG and diode lasers.

8. The method of claim 1 wherein the laser beam is focused at a site on the skin with a diameter of 0.1 - 5. 0 mm.

9. The method of claim 1 wherein the energy fluence of the laser beam at the skin is 0.03 -100,000 J/cm².

10. The method of claim 1 wherein the energy fluence of the laser beam at the skin is 0.03 - 9.6 J/cm².

11. The method of claim 1 wherein multiple ablations are made to prepare the skin for diffusion of interstitial fluid.

12. The method of claim 1 wherein multiple ablations are made to prepare the skin for pharmaceutical delivery.

13. The method of claim 1 further comprising a beam splitter positioned to create, simultaneously from the laser, multiple sites of ablation.

14. The method of claim 13 wherein the beam splitter is selected from a series of partially silvered mirrors, a series of dichroic mirrors, and a series of beam-splitting prisms.

15. The method of claim 1 further comprising an acousto-optic modulator outside the laser cavity wherein the modulator consecutively deflects the beam at different angles to create different sites of ablation on the skin.

16. The method of claim 1 wherein the analyte to be measured is selected from the group consisting of Na⁺, K⁺, Ca⁺⁺, Mg⁺⁺, Cl⁻, HCO₃⁻, HHCO₃, phosphates, S4, glucose, amino acid, cholesterol, phospholipids, neutral fat, PO₂, pH, organic acids or proteins.

17. The method of claim 1 wherein the analyte measurement is used to represent the analyte concentration in blood.

18. The method of claim 1 wherein the interstitial fluid is collected in a container positioned proximal to the ablation site and through which the laser beam passes.

19. The method of claim 18 wherein the testing of analyte concentration is conducted while the container unit is attached to the laser device.

20. The method of claim 1 further comprising the step of applying a therapeutically effective amount of a pharmaceutical composition at the site of ablation.

21. The method of claim 20 wherein the pharmaceutical substance is administered based on analyte concentration in the interstitial fluid.

22. The method of claim 1 further comprising the step of applying a pressure gradient to the skin after formation of the site of ablation to increase the diffusion rate of interstitial fluid..

23. The method of claim 1 further comprising the step of mechanically increasing the diffusion rate of interstitial fluid after formation of a site of ablation.

24. The method of claim 23 wherein diffusion is increased by the application of subatmospheric pressure at the ablation site.

25. The method of claim 24 wherein the container unit is under subatmospheric pressure.

26. The method of claim 1 wherein a pressure gradient is created at the site of ablation to increase the removal of bodily fluids.

27. A method of measuring analyte concentrations in bodily fluids, comprising the steps of:

- a) focusing a laser beam with sufficient energy fluence to alter the skin at least as deep as the stratum corneum, but not as deep as the capillary layer; and
- b) firing the laser to create a site of alteration, the site having a diameter of between 0.5 microns and 5.0 cm.
- c) collecting a sample of interstitial fluid released by steps (a) and (b); and
- d) testing the fluid for analyte concentration.

28. The method of claim 27 wherein the laser beam has a wavelength of 0.2-10 microns.

29. The method of claim 27 wherein the laser beam has a wavelength of between 1.5-3.0 microns.

30. The method of claim 27 wherein the laser beam has a wavelength of about 2.94 microns.

31. The method of claim 27 wherein the laser beam is emitted by a laser selected from the group consisting of Er:YAG, pulsed CO₂, Ho:YAG, Er:YAP, Er/Cr:YSGG, Ho:YSGG, Er:GGSG, Er:YLF, Tm:YAG, Ho:YAG, Ho/Nd:Y_{AlO₃}, cobalt:MgF₂, HF chemical, DF chemical, carbon monoxide, deep UV lasers, and frequency tripled Nd:YAG lasers.

32. The method of claim 27 wherein the laser beam is emitted by an Er:YAG laser.

33. The method of claim 27 wherein the laser beam is emitted by a modulated laser selected from the group consisting of continuous-wave CO₂, Nd:YAG, Thallium:YAG and diode lasers.

34. The method of claim 27 wherein the laser beam is focused at a site on the skin with a diameter of 0.1 - 5.0 mm.

35. The method of claim 27 wherein the energy fluence of the laser beam at the skin is 0.03 - 100,000 J/cm².

36. The method of claim 27 wherein the energy fluence of the laser beam at the skin is 0.03 - 9.6 J/cm².

37. The method of claim 27 wherein multiple alterations are made to prepare the skin for diffusion of interstitial fluid.

38. The method of claim 27 wherein multiple alterations are made to prepare the skin for pharmaceutical delivery.

39. The method of claim 27 further comprising a beam splitter positioned to create, simultaneously from the laser, multiple sites of alteration.

40. The method of claim 39 wherein the beam splitter is selected from a series of partially silvered mirrors, a series of dichroic mirrors, and a series of beam-splitting prisms.

41. The method of claim 27 further comprising an acousto-optic modulator outside the laser cavity wherein the modulator consecutively deflects the beam at different angles to create different sites of alteration on the skin.

42. The method of claim 27 wherein the analyte to be measured is selected from the group consisting of Na^+ , K^+ , Ca^{++} , Mg^{++} , Cl^- , HCO_3 , HHCO_3 , phosphates, S^4- , glucose, amino acid, cholesterol, phospholipids, neutral fat, PO_2^- , pH, organic acids or proteins.

43. The method of claim 27 wherein the analyte measurement is used to represent the analyte concentration in blood.

44. The method of claim 27 wherein the interstitial fluid is collected in a container positioned proximal to the ablation site and through which the laser beam passes.

45. The method of claim 27 wherein the testing of analyte concentration is conducted while the container unit is attached to the laser device.

46. The method of claim 27 further comprising the step of applying a therapeutically effective amount of a pharmaceutical composition at the site of alteration.

47. The method of claim 46 wherein the pharmaceutical substance is administered based on analyte concentration in the interstitial fluid.

48. The method of claim 27 further comprising the step of applying a pressure gradient to the skin after formation of the site of ablation to increase the diffusion rate of interstitial fluid.

49. The method of claim 27 further comprising the step of mechanically increasing the diffusion rate of interstitial fluid after formation of a site of alteration.

50. The method of claim 49 wherein diffusion is increased by the application of sub-atmospheric pressure at the alteration site.

51. The method of claim 50 wherein the container unit is under subatmospheric pressure.

52. The method of claim 27 wherein a pressure gradient is created at the site of alteration to increase the removal of bodily fluids.

53. A method of measuring analyte concentration in bodily fluids, comprising the steps of:

- a) applying sub-atmospheric pressure at the surface of the skin to induce the formation of a microblister;
- b) focusing a laser beam with sufficient energy fluence to lyse a microblister;
- c) firing the laser to lyse the blister;
- d) collecting a sample of interstitial fluid released by steps (a), (b) and (c);

and

- e) testing the fluid for analyte concentration.

54. The method of claim 53 wherein the laser beam has a wavelength of 0.2-10 microns.

55. The method of claim 53 wherein the laser beam has a wavelength of between 1.5-3.0 microns.

56. The method of claim 53 wherein the laser beam has a wavelength of about 2.94 microns.

57. The method of claim 53 wherein the laser beam is emitted by a laser selected from the group consisting of Er:YAG, pulsed CO₂ Ho:YAG, Er:YAP, Er/Cr:YSGG, Ho:YSGG, Er:GGSG, Er:YLF, Tm:YAG, Ho:YAG, Ho/Nd:Yal₀3, cobalt:MgF₂, HF chemical, DF chemical, carbon monoxide, deep UV lasers, and frequency tripled Nd:YAG lasers.

58. The method of claim 53 wherein the laser beam is emitted by an Er:YAG laser.

59. The method of claim 53 wherein the laser beam is emitted by a modulated laser selected from the group consisting of continuous-wave CO₂, Nd:YAG, Thallium:YAG and diode lasers.

60. The method of claim 53 wherein the laser beam is focused at a site on the skin with a diameter of 0.1 - 5.0 mm.

61. The method of claim 53 wherein the energy fluence of the laser beam at the skin is 0.03 -100,000 J/cm².

62. The method of claim 53 wherein the energy fluence of the laser beam at the skin is 0.03 - 9.6 J/cm².

63. The method of claim 53 wherein multiple microblisters are made for collection of interstitial fluid.

64. The method of claim 53 further comprising a beam splitter positioned to lyse, simultaneously from the laser, multiple microblisters.

65. The method of claim 64 wherein the beam splitter is selected from a series of partially silvered mirrors, a series of dichroic mirrors, and a series of beam-splitting prisms.

66. The method of claim 53 further comprising an acousto-optic modulator outside the laser cavity wherein the modulator consecutively deflects the beam at different angles to lyse different microblisters.

67. The method of claim 53 wherein the analyte to be measured is selected from the group consisting of Na⁺, K⁺, Ca⁺⁺, Mg⁺⁺, Cl⁻, HCO₃⁻, HHCO₃, phosphates, S4⁻, glucose, amino acid, cholesterol, phospholipids, neutral fat, PO₂⁻, pH, organic acids or proteins.

68. The method of claim 53 wherein the analyte measurement is used to represent the analyte concentration in blood.
69. The method of claim 53 wherein the interstitial fluid is collected in a container positioned proximal to the microblister and through which the laser beam passes.
70. The method of claim 53 wherein the testing of analyte concentration is conducted while the container unit is attached to the laser device.
71. The method of claim 53 further comprising the step of applying a therapeutically effective amount of a pharmaceutical composition at the site of the lysed microblister.
72. The method of claim 71 wherein the pharmaceutical substance is administered based on analyte concentration in the interstitial fluid.